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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/087,411	03/01/2002	Gary P. Schroth	9584-030-999	6226
20583	7590	02/02/2006	EXAMINER	
JONES DAY 222 EAST 41ST ST NEW YORK, NY 10017			SITTON, JEHANNE SOUAYA	
			ART UNIT	PAPER NUMBER
			1634	
DATE MAILED: 02/02/2006				

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/087,411	<b>Applicant(s)</b> SCHROTH, GARY P.	
	<b>Examiner</b> Jehanne S. Sitton	<b>Art Unit</b> 1634	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 21 December 2005.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,2,5-7,9-12 and 21-25 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-2, 5-7, 9-12, and 21-25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

1. Currently, claims 1-2, 5-7, 9-12, and 21-25 are pending in the instant application. The following rejections are maintained. They constitute the complete set being presently applied to the instant Application. Response to applicant's arguments follow. This action is FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### ***Claim Rejections - 35 USC § 103***

3. Claims 1-2, 5-7, 9-12, and 21-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chee (Chee et al; US Pregrant Publication 2002/0132221) in view of Collins.

With regard to claims 1, 2 and 7, Chee teaches a method involving decoding an array composition comprising providing an array (instant claim 12) which contains populations of microspheres or beads (coded test unit, coded substrate) which each comprise at least a first and a second subpopulation comprising a bioactive agent and an identifier binding ligand (coding oligonucleotide) which binds to a decoder binding ligand (decoding oligonucleotide), and adding the decoder binding ligand to the array to identify the location of the bioactive agents (see para 0014-0018). Chee teaches that the bioactive agent (instant claim 9) and binding ligands can be nucleic acids (para 0039) which are particularly preferred (para 0040). With regard to instant claim 21, Chee teaches that the bioactive agent can also be a protein (para 0042). Chee teaches that decoding occurs through the use of the decoding binding ligands that are added during the decoding step wherein the decoding binding ligand (DBL) bind either to a distinct identifier

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binding ligand (IBL) that is placed on the beads or to the bioactive agent itself (para 0023). Chee teaches that the array can contain only a single bead for each bioactive agent (plurality of coded test units, plurality of coded substrates), or a plurality of beads of each type (plurality of coded test units, plurality of coded substrates) (para 0035) and teaches the use of a library of bioactive agents (para 0045). Chee teaches that preferably the IBL – identifier probe and DBL-decoder probe, are nucleic acids and that the probes should be specific so as to distinguish different IBL-DBL pairs (para 0069). Chee teaches that each subpopulation of beads comprises a plurality of different IBLs and that by using different IBLs to encode each bioactive agent, the number of possible unique codes for each agent is increased (para 0074, instant claim 24). Chee teaches that the DBL can carry a label such as a flourophore (para 0068), and are preferably directly or indirectly labeled (para 0101) such that the identification of the location of individual beads (or subpopulation of beads) is carried out in the presence of the IBL (para 0102-0104, “decoding oligonucleotide produces a detectable hybridization signal sufficient to distinguish the coded test unit from the plurality of coded test units”). Chee teaches that attachment of the nucleic acids to the beads can be covalent (claims 6 and 23; para 0051). Chee teaches that the bioactive agent and IBL can be different nucleic acids which are each independently linked to the bead (claims 11 and 25; para 0014, 0021). With regard to claim 10, Chee teaches that alternatively, the test moiety and coding oligonucleotide can be a single polynucleotide (para 0071), in such case the test moiety and the coding oligonucleotide can be considered to be covalently linked (claim 22).

With regard to claims 1 and 5, although Chee teaches the use of isoguanine, isocytosine, Xanthanine, and hypoxanthanine (para 0047) as nucleic acid analogs, and suggests the use of such in the nucleic acids and probes of the invention taught by Chee, Chee does not specifically

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teach the use of such orthogonal nucleobases in the decoding binding ligand. Chee, however, does teach that the DBL-IBL nucleic acid pairs should be specific (para 0100). Collins teaches that orthogonal nucleobases such as iso-G, iso-C, or K, can be used to reduce nonspecific binding and non specific hybridization in hybridization assays (col. 15, lines 1-21). Collins teaches that such can be applied to the use of probes on solid supports (col. 15, lines 30-33). Collins teaches that using such non natural nucleobases adds to the diversity of a library of possible sequences and enables the design of universal sequences that are as noninteracting as possible among themselves (col. 25, lines 35-45). Collins specifically teaches and demonstrates the use of such nucleobases in methods involving the reduction of non specific hybridization for the detection of target polynucleotides of interest. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the DBL-IBL nucleic acids of Chee with the use of orthogonal nucleobases, such as iso-G, iso-C, X, H, or K, as suggested by Chee and specifically taught by Collins, for the purpose of increasing the specificity of the DBL-IBL nucleic acid pairs in the decoding method of Chee. The ordinary artisan would have been motivated to provide optimal specificity for the DBL-IBL method of Chee because Chee teaches that the DBL-IBL nucleic acid pairs should be specific for each other. The ordinary artisan would have been motivated to optimize specificity of the DBL-IBL nucleic acid pairs of Chee with orthogonal nucleobases as used by Collins, because Collins specifically teaches that these nucleobases can be used to reduce non specific binding and hybridization in nucleic acid hybridization assays.

*Response to Arguments*

4. The response traverses the rejection. The response asserts that the motivation alleged by the Patent Office to “optimize specificity” of certain nucleic acids discussed by Chee by including orthogonal as described by Collins cannot be found either expressly or implicitly in the statements of either reference. The response asserts that Chee teaches the use of orthogonal nucleobases not “in the context of DBL-IBLs” but in nucleic acid bioactive agents. This argument has been thoroughly reviewed but was not found persuasive. As stated in MPEP 2144 “The rationale to modify or combine the prior art does not have to be expressly stated in the prior art; the rationale may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art...”. While neither reference explicitly teaches to use orthogonal nucleobases in the DBL-IBL pairs of Chee, Chee does teach the use of orthogonal nucleobases in the context of nucleic acids which are defined as “at least two nucleotides covalently linked together” (para 0047) and teaches that nucleic acids can have any combination of bases including orthogonal nucleobases (end of para 0047). This definition is not limited to the bioactive agent, and Chee teaches that the DBL and IBL can be nucleic acids (para 0100) and also teaches that in some embodiments the IBL and bioactive agent are the same moiety (para 0071). Although with regard to specificity, Chee teaches optimization with length of IBL-DBL probes (para 0069), as noted in the MPEP, chapter 2123, “Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or non preferred embodiments. In re Susi, 440 F.2d, 169 USPQ 423 (CCPA 1971)”. At the time the invention was made, a number of different ways were known in the prior art to optimize hybridization specificity between nucleic acids, including length of nucleic acid probes,

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GC content, salt concentration, temperature, and as exemplified by Collins, the use of orthogonal nucleobases. Collins specifically teaches that orthogonal nucleobases such as iso-C and iso-G can be used to minimize non specific hybridization and non specific binding (col. 12, lines 43-43) in nucleic acid hybridization, increase accuracy of detection in nucleic acid hybridization assays (col. 2, lines 43-44), allow more precise control over hybridization (col. 3, lines 28-29), due to an expanded “alphabet” of bases, as well as teaching the use of such with hybridization on supports (col 15, lines 32-33).

The response further asserts that Chee teaches the DBL and IBL should bind with a specificity sufficient to differentiate the DBL from other DBLs and teaches specific dissociation constants (para 0065). The response asserts that the Patent Office has not demonstrated why one of skill in the art would be motivated to optimize specificity of the system in Chee that is already highly specific. This argument has been thoroughly reviewed but was not found persuasive. At para. 0065, Chee does not specifically teach how to achieve specificity. Although at para 0069, as pointed to in the response, Chee exemplifies specificity with length of IBL-DBL pairs (para 0069), as noted in the MPEP, chapter 2123, “Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or non preferred embodiments. In re Susi, 440 F.2d, 169 USPQ 423 (CCPA 1971)”. Therefore, the responses assertion at the last para of page 6 of the response that Chee indicates to those of skill in the art that “optimal specificity can be found with adjusting probe length alone” is not found persuasive. Such statement does not address the teachings of Chee as a whole as well, or the teaching of alternative embodiments of the make-up of nucleic acids that are specifically taught by Chee to encompass orthogonal nucleobases. At the time the invention was made, a number of different ways were known to

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optimize specificity, including length of nucleic acid probes, GC content, salt concentration, temperature, and as exemplified by Collins, the use of orthogonal nucleobases. Collins specifically teaches that orthogonal nucleobases such as iso-C and iso-G can be used to minimize non specific hybridization and non specific binding (col. 12, lines 43-43) in nucleic acid hybridization, increase accuracy of detection in nucleic acid hybridization assays (col. 2, lines 43-44), allow more precise control over hybridization (col. 3, lines 28-29), due to an expanded “alphabet” of bases, as well as teaching the use of such with hybridization on supports (col 15, lines 32-33).

The response asserts that with the use of orthogonal nucleobases, one of skill might arrive at probes that are too specific for the method of Chee. This argument has been thoroughly reviewed but was not found persuasive. The response provides no explanation of how the IBL-DBL pairs of Chee could be “too specific”. Chee teaches that each probe should bind to it’s corresponding decoder probe. Thus, it is clear that the specificity should be achieved such that each probe binds to it’s corresponding decoder probe, and that non specific hybridization must be avoided. It is unclear how probes could be too specific. Either they specifically bind to their corresponding decoder probe, or they don’t and render the decoding step useless. Further, Chee specifically teaches the parameters for specificity at paragraph 0069, stating that the IBL-DBL pairs should “allow both a) dissociation, if necessary; and b) efficient hybridization”, and teaches dissociation constants at para 0065. Also, Collins teaches how the orthogonal nucleobases affect specificity. Therefore, given the teachings of Chee and Collins, the knowledge required to achieve appropriate specificity was provided by the prior art. Although Chee exemplifies specificity with the use of probe length, the state of the art at the time the invention was made



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taught that specificity optimization included a number of different factors, including the use of orthogonal nucleobases, which Chee suggests to use in the context of nucleic acids. Therefore, not only does Chee suggest the use of orthogonal nucleobases in the context of nucleic acids and teaches that DBL-IBL probes can be made up of nucleic acids, but Collins provides ample motivation for the use of orthogonal nucleobases in nucleic acid hybridization to minimize non specific hybridization and non specific binding, increase accuracy of detection in nucleic acid hybridization assays, and allow more precise control over hybridization through the use of an expanded “alphabet” of bases. For these reasons and the reasons already made of record, the rejection is maintained.

### ***Conclusion***

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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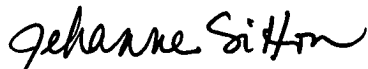
6. No claims are allowable over the cited prior art.
7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0752. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272-0745. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.



Jehanne Sitton  
Primary Examiner  
Art Unit 1634

1/31/06